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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,562	07/17/2003	Zhizhen Zeng	PF530C1	3320

22195 7590 03/24/2006

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,562	ZENG ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/03 & 2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 22-31 are pending in the instant application. Claims 1-21 have been canceled and claims 22-31 have been added as requested by Applicant in the Paper filed January 6, 2006.

Election/Restrictions

2. Applicant's election of group II drawn to polypeptides and further election ofTR21 polypeptides in the reply filed on January 6, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

All claims are currently under examination.

Priority

3. This application filed under former 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/910,562. A statement reading "(now abandoned)" should be included after "09/910,562, filed on July 23, 2001" following the title in the first sentence of the specification.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 22-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Claims

22-31 are directed to the protein of SEQ ID NO: 2, identified as TR21. The instant specification discloses that TR21 is a 271 amino acid protein, and asserts that it is a member of the tumor necrosis factor family of receptors, due to structural homology to that family of receptors and the presence of cysteine-rich motifs. However, the protein does not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The instant application states that functional activities of the TR21 polypeptide are biological activity, antigenicity, immunogenicity, ability to form multimers with TR21 polypeptides of the invention, and ability to bind to a receptor or ligand for a TR21 polypeptide. There is no evidence presented or statement made that any specific ligand actually binds to or interacts with the TR21 protein. These are general activities that would apply to virtually any protein in the tumor necrosis receptor family, and are not specific to this particular protein. The specification also describes the uses and methods of the invention, in which the proteins and nucleic acids can be used in methods such as screening assays to identify ligands, receptors, binding proteins, agonists or antagonists, to raise monoclonal or polyclonal antibodies, use of the nucleic acid to screen libraries of DNA or to make fusion proteins or to identify chromosomes or location of particular sites on a chromosome, making transgenic or knockout animals to use as animal model systems to determine the effects of TR21 or to screen for compounds, expressing the nucleic acid in order to make the protein, or to determine tissue expression by Northern blotting, for example, or to use the TR21 protein in bioassays to determine the effect of the protein on various biological activities, such as on stimulated proliferation and/or differentiation

on cells, stimulation of endothelial migration, wound healing, or angiogenesis for example, as described in Examples 15-38.

However, none of these uses are considered to be specific or substantial utilities for either the protein or the encoding nucleic acid molecules. Methods such as identification of ligands, use to screen for homologous genes, use to identify chromosomes or chromosomal location, use to recombinantly produce protein or fusion proteins or use to generate antibodies are considered general methods applicable to any protein and/or nucleic acid, and are not considered specific or substantial. Use of TR21 in bioassays is also not a specific and substantial utility, and is only further research to discover what the activities and biological significance of the protein is. Additionally, the specification teaches on page 9 that transient expression of transfected TR21 DNA in 293T cells, in the presence of a NF-κB-SEAP reporter construct, activated the NF-κB transcription complex in a dose dependent manner, indicating that TR21 plays a role as a cellular proliferative factor. While this result indicates that ectopically expressed TR21 has this activity, many other proteins also activate this transcription factor, and this information is part of the process of determining what the specific biological activity of this protein is and is a starting point for further research.

The instant application also teaches that the protein and nucleic acids, associated antibodies, agonists, antagonists and antisense nucleic acids can be used either diagnostically to detect abnormal levels of the TR21 protein or nucleic acids, identify mutations, disorders or diseases, or prophylacticly or therapeutically to treat diseases or disorders, such as those listed throughout the specification and especially on pages 40, 117-118, 121-124 and 127-135, and include diseases, disorders or infections such as immune system disorders, viral, fungal, parasitic

or bacterial infectious disease, graft-host disease, immunodeficiency, autoimmune diseases and the like, cancers, AIDS, neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Retinitis pigmentosa among others, myelodysplastic syndromes such as aplastic anemia, ischemic injury such as caused by stroke or myocardial infarction, toxin-induced liver disease, septic shock, cachexia and anorexia, cardiovascular disorders, cerebrovascular disorders, blood-composition-affecting disorders, or can be used for the expansion of immature hematopoietic progenitor cells and as a modulator or hematopoietic stem cells in vitro for the purpose of bone marrow transplantation and/or gene therapy, and to boost the immune system, among others listed.

However, the assertions that the protein and/or nucleic acids of the instant invention can be used in the diagnosis or treatment of diseases or disorders, or to boost the immune system, are based on both the tissue expression of TR21 (preferentially expressed in fetal liver and spleen, and to a lesser extent in bone marrow, umbilical vein and T cells) and the assumption that the proteins are receptors in the tumor necrosis factor receptor family, which as a family are involved in myriad biological pathways and immune activities and disorders, and therefore are not a specific and substantial utilities. Many proteins are members of evolutionarily related families, yet have diverse biological activities and functions. The members of the tumor necrosis receptor family bind distinct ligands and have specific biological activities. There is no ligand known to bind and activate the TR21 protein, and the biological activities upon ligand binding are also not known for this protein.

There is no nexus between any of the diseases or disorders and the molecules of the

instant invention. Given no disease state or any other function or activity known for the protein, the protein is not considered to have utility. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a nucleic acid molecule encoding a protein which has undetermined function or biological significance, and the use of an orphan receptor to discover its ligand or properties does not constitute a specific, substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be some specific and substantial activity or function known. It is possible that after further characterization, this protein might be found to have a patentable utility, such as association with a specific disease. This further characterization, however, is part of the act of invention, and until it has been undertaken the Applicants' claimed invention is incomplete. Because there is no specific and substantial utility asserted, credibility cannot be assessed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5.1 Claims 22-31 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use it.

5.2 Claims 22 and 26-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants' referral to the deposits of clone HCFMV39 on page 5 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposits will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

Pertinent Art

6. The art considered pertinent to the present application is Tang et al., WO2003025148, March 27, 2003, which discloses a polypeptide (SEQ ID NO: 350) which is identical to the polypeptide of SEQ ID NO: 2 of the present application. This is not considered prior art, as the effective filing date is after that of the instant application.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER